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High risk for sleep apnea in the Berlin questionnaire and coronary artery disease

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Abstract
Introduction Obstructive sleep apnea (OSA) affects up to 30% of the adult population and is a risk factor for coronary artery disease (CAD). The diagnostic process, involving polysomnography, may be complex. Berlin questionnaire (BQ) is a validated and economical screening tool.
Purpose The aim of this study was to assess the performance of the BQ for the diagnosis of OSA in individuals with angina complaints.
Methods Patients undergoing diagnostic cineangiography, portable type III polysomnography to determine the apnea-hypopnea index (AHI), and who answered the BQ were included. We excluded patients older than 65 years that were smokers, diabetics, and morbidly obese. High risk for OSA was based on positive responses in two of three symptom criteria of the BQ. CAD was defined by the presence of >50% lesion in coronary arteries.
Results In 57 included cases, high risk in the BQ indicates significant odds ratio [95% confidence interval] for the presence of CAD (4.5[1.03–19.25], P=0.045), adjusted for usual confounders: gender, age, and body mass index. The sensitivity and the specificity of BQ for CAD were 70% and 48%, respectively; the positive and negative predictive values are 56% and 64%.
Conclusions In conclusion, simple questionnaire-based diagnostic tools can be included in the screening procedures of patients with angina to detect the need for further OSA

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evaluation. In conclusion, the BQ is an effective instrument for this purpose.

Keywords Sleep apnea syndromes · Sleep monitoring · Questionnaire · Coronary artery disease

Introduction

Obstructive sleep apnea (OSA) affects up to one-third of adult population [1–3] and is often associated with cardiovascular disease [4–10], diabetes [11, 12], and mortality [13–19]. Obesity [20, 21], advanced age [22], and gender [23, 24] are involved in OSA pathophysiology [25, 26]. These factors are similar to the ones implicated in coronary artery disease (CAD) [27].

In no other field than cardiology, the need to recognize OSA is so urgent. [28–30] Studies have shown the potential benefit of diagnosis and treatment of OSA in reducing cardiovascular events, and thus, mortality [20, 31–34]. As long as the diagnosis of OSA remains complex, expensive, and time-consuming, the subset of diagnosed cases will be minority.

Polysomnography (PSG) is the golden standard for the diagnosis of sleep apnea [35]. Portable home monitoring with type III PSG monitors is an alternative to make OSA diagnosis more readily available in different clinical circumstances [36–39]. A simpler alternative for the diagnosis of OSA may be the use of validated questionnaires. [40–42] The questions in BQ were selected from studies of risk factors or behaviors that consistently predict the presence of sleep apnea. By consensus, the instrument is focused on a limited group of known risk factors for sleep apnea [43].

The assessment of simplified OSA diagnostic methodologies is still incipient and has not been explored in depth in the ambit of cardiology. The aim of the present study is to evaluate the feasibility of utilizing the BQ for the diagnosis of sleep apnea in angina patients.

Methods

This study is a secondary analysis of data collected as previously described [44]. A cross-sectional study was conducted between March 2007 and February 2008, screening 519 consecutively angina patients referred by their physicians for diagnostic coronary angiography. The exclusion criteria were: age >65 years; smoking in the previous 6 months; clinical diagnosis; dietary, or pharmacological treatment for diabetes mellitus; anginous pain in the previous week; use of anxiolytic medication; treatment for chronic pulmonary disease; body mass index (BMI) >40 kg/m^2; any physical, psychological, or social issue encumbering the attainment of the home polysomnographic monitoring; and previous coronary intervention (myocardial revascularization or angioplasty). A full medical history was taken from all study participants. The project was approved by the institutional ethics committee, and all participants signed an informed consent form.

The volunteers underwent portable PSG at home, using a level III monitor (SOMNOcheck Effort, Weinmann, Germany), a procedure validated by our group [37]. Air flow and snoring were measured through a nasal cannula connected to a pressure transducer. In addition, inspiratory effort, pulse oximetry, heart rate, and sleep position were measured. The records were made at the patient's home, usually between 11 P.M. and 7 A.M. The records were scored by a board-certified sleep specialist in a different location, blind to the other results.

Apneas were defined as airflow reduction to 10% or less of the baseline value for 10 s or more; hypopneas as airflow reduction of 50% or more, associated with 3% or more reduction of oxygen saturation (SaO_2). Central and

Table 1 Clinical and polysomnographic characteristics in patients with low and high risk for sleep apnea by the Berlin questionnaire

Characteristics	Low risk n=23	High risk n=34	Total n=57	p value
Gender Male (%)	39	50	46	0.5
Age (years)	54±8.2	54±6.1	54±6.9	0.9
Weight (kg)	76±13	76±12	76±12	0.9
BMI (kg/m^2)	23±4.0	22±10	23±11	0.8
SBP (mmHg)	139±28	144±12	142±23	0.6
DBP (mmHg)	81±16	86±11	83±13	0.5
CAD (n)	8	19	27	0.2
AHI (events/h)	16±13	18±15	17±14	0.6
AHI≥15 (%)	30	53	44	0.1
AHI≥5 (%)	83	76	79	0.6
Lowest SaO_2	85±6.3	86±3.7	86±4.9	0.5
Lowest SaO_2≤85 (%)	41	30	35	0.4

Data presented as mean±SD or n and percentage. *BMI* Body mass index, weight divided by height squared (Kg/m^2). *AHI* Apnea-hypopnea index, expressed by events per hour; *CAD* coronary arterial disease; *SBP* systolic blood pressure; *DBP* diastolic blood pressure

Variable	Risk factors for coronary artery disease OR	CI 95%	Risk factors for obstructive sleep apnea OR	CI 95%
Berlin Questionnaire (high risk, 1)	4.5	1.03 – 19.25; ***p= 0.045***	4.69	1.21 – 18.2; ***p= 0.026***
BMI (Kg/m^2)	1.01	0.85 – 1.19; p= 0.90	0.91	0.78 – 1.07; p= 0.27
Gender (Male, 1)	4.12	1.10 – 15.35; ***p= 0.035***	2.75	0.81 – 9.43; p= 0.10
Age (years)	1.16	1.04 – 1.29; ***p= 0.009***	1.09	0.99 – 1.2; p= 0.074

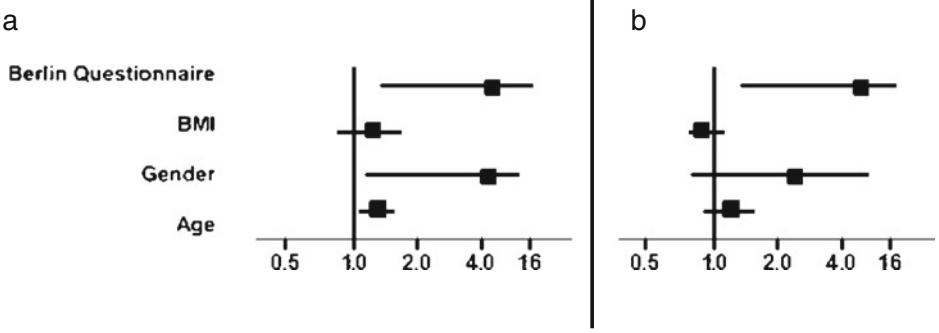

Fig. 1 Results of the binary logistic regression for estimating the odds ratio of coronary artery disease and obstructive sleep apnea, adjusted for risk factors; *BMI* body mass index; *OR* odds ratio; *CI* confidence interval; significant p values are in bold type

obstructive apneas were defined by the absence or presence of thoracic and abdominal movements. AHI was calculated by dividing the total apneas and hypopneas by the number of hours and classified in: normal AHI/h<5; mild AHI/h from 5 to 14; moderate AHI/h from 15 to 29; severe AHI/h≥30 [45, 46].

All patients were assessed in routine quantitative angiography, using the same equipment (Siemens D40) and projection, with the table and image intensifier kept at constant height. Image quantification was carried out in all cases by the same investigator, who was blinded to laboratory and PSG results. A magnification of 7 in. was used for all images. Significant CAD was defined as ≥50% of luminal narrowing of at least one coronary segment. Patients with no lesion or with lesions ≤50% of luminal narrowing were considered as controls.

The Berlin questionnaire (BQ) has been described in detail elsewhere [40]. In brief, the questions are one about weight gain, four related to snoring, three about sleep during the day, one related to car driving, and one about hypertension. The OSA risk determination was based on the following criteria: category 1, persistent symptoms (3 to 4 times a week) in two or more questions on snoring; category 2, persistent (3 to 4 times a week) tiredness after waking, drowsiness while driving, or both; and category 3, history of hypertension. To be considered high risk for OSA, the patient should fulfill criteria in at least two categories of the symptoms. Those classified in only one category were allocated to the low-risk group.

Scalar data were expressed as mean ± standard deviation. Differences between means were compared using Student's t test. Chi-square test was used to estimate the odds ratio of CAD and of OSA in face of a high risk in BQ. Binary logistic regression was used to adjust for age, gender, and BMI; the odds ratio of CAD and OSA when BQ is high risk. Sensitivity, specificity, positive and negative predictive value were calculated by apnea-hypopnea index (AHI)≥15/h as the cut point for OSA. Data were analyzed using SPSS for Windows v16 (SPSS Chicago, IL, USA) and EBM Calculator Version 1.2. The significance level for alpha error was p<0.05 for all analysis.

Results

Characteristics of the sample are shown in Table 1. The association between high risk for OSA in BQ and CAD is non-significant. In a logistic regression model, however,

Table 2 Diagnostic performance of the Berlin questionnaire to predict coronary artery disease and higher apnea-hypopnea index (% and 95% CI)

	Berlin high risk for predicting	
	CAD	AHI≥15/h
Sensitivity	70 (51.5–84.1)	72 (52.4–85.7)
Specificity	48 (31.4–65.6)	50 (33.6–66.4)
PPV	56 (39.5–71.1)	53 (36.7–68.5)
NPV	64 (43.0–80.3)	70 (49.1–84.4)

AHI apnea-hypopnea index; *OSA* obstructive sleep apnea syndrome; *CAD* coronary artery disease; *CI* confidence interval; *NPV* negative predictive value; *PPV* positive predictive value

adjusting for gender, age, BMI, odds ratio for CAD when BQ indicates high risk for OSA was significant. Patients with BQ high risk are 4.5 times more likely having CAD, regardless of age, gender, and BMI (Fig. 1).

The association between high risk for OSA in BQ and the AHI in the portable monitoring, is non-significant, either as continuous variable, or as binary variable, either using a cut point of ≥5/h or of ≥15/h. After adjusting for age, gender, and BMI, the high risk for in BQ becomes significantly associated to AHI≥15 (Fig. 1).

The diagnostic performance of the BQ to predict CAD and AHI≥15 is shown in Table 2. Both the CAD and the AHI≥15 are similarly detectable by the BQ. The 95% sensitivity and specificity are shown and depict the modest but adequate diagnostic ability of the questionnaire.

Discussion

Our study has shown that 56% of subjects with CAD are at high risk for OSA in the BQ. The association between a high-risk status in the questionnaire and CAD became apparent only after controlling for the classical confounders of OSA. Therefore, the clinical applicability of the instrument in patients with CAD is still not resolved.

The association between OSA and CAD has been demonstrated in different study populations [5–7]. The golden standard for diagnosis of OSA, full night, in-laboratory PSG, is scarcely accessible in most centers, and for various reasons has not gained routine status in cardiology [47, 48]. Thus, alternative tools, simpler and more affordable, should be used in the OSA screening and diagnosis [43]. The results must be confirmed in larger populations, encompassing all risk factors for CAD, since the selection criteria employed to avoid oxidative stress limit the results.

The BQ in our study has significance in predicting AHI at the cutoff point ≥15/h also only after controlling for confounders. The BQ was created in 1996 and was validated in 1999 [40]. No evaluation of the diagnostic performance of the BQ on the Brazilian general population is published. Our group has investigated the application of the BQ in the cardiology setting [42]. It is beyond the scope of the present study to validate the BQ against other methods.

One limitation of our study is the fact that AHI was measured by portable home monitoring. This method underestimates in approximately 10% of the AHI and has its lowest area under the ROC curve at the cutoff point of 15/h used in the present study [37]. Additional limitations of the study in terms of sample size and selection do not encumber the conclusion regarding the clinical usefulness of the BQ in the catheterization room. The levels of specificity, sensitivity, positive predictive value, and negative predictive value of the BQ against portable PSG were adequate for a test so unpretentious and inexpensive.

Similar diagnostic performance of the BQ was described in different settings [49]. A population of the outpatient hypertension clinic was assessed by portable monitoring and BQ. The ability of the BQ to predict resistant hypertension was similar to the AHI>10 [42]. Furthermore, we had no difficulty to administer the questionnaire, although the patient population was selected in a public teaching hospital. The BQ is feasible even through telephone interviews [50].

In summary, high risk for OSA assessed by the BQ is highly prevalent in cardiac patients and is associated with CAD. Therefore, as a first step in the investigation, before more complex OSA diagnostic methods are employed, assessing patients with cardiovascular disease by the BQ can be useful.

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Conflict of interest None.

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